updated search LJC 10/9/02

```
=> s (ser cit his)
L1            0 (SER CIT HIS)

=> s`citrullination?
L2           34 CITRULLINATION?

=> s duplicate remove l2
MISSING OPERATOR REMOVE L2
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> duplicate remove l2
DUPLICATE PREFERENCE IS 'BIOSIS, CAPLUS, EMBASE, MEDLINE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L2
L3            14 DUPLICATE REMOVE L2 (20 DUPLICATES REMOVED)

=> d l3 1-14 all

L3   ANSWER 1 OF 14  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
     1
AN   2002:315329  BIOSIS
DN   PREV200200315329
TI   Autoantigenic posttranslational modifications of proteins: Does it apply
     to rheumatoid arthritis.
AU   Zhou, Zhijie; Menard, Henri-Andre (1)
CS   (1) McGill University Health Center, 1650 Cedar Avenue, Suite A6.162,
     Montreal, PQ, H3G 1A4: henri.a.menard@muhc.mcgill.ca Canada
SO   Current Opinion in Rheumatology, (May, 2002) Vol. 14, No. 3, pp. 250-253.
     http://www.co-rheumatology.com/. print.
     ISSN: 1040-8711.
DT   Article; General Review
LA   English
CC   Biochemical Studies - General  *10060
     Bones, Joints, Fasciae, Connective and Adipose Tissue - Pathology  *18006
     Immunology and Immunochemistry - General; Methods  *34502
     Immunology and Immunochemistry - Immunopathology, Tissue Immunology
     *34508
     Allergy  *35500
BC   Animalia - Unspecified   33000
     Hominidae   86215
     Muridae   86375
IT   Major Concepts
        Biochemistry and Molecular Biophysics; Clinical Immunology (Human
        Medicine, Medical Sciences); Rheumatology (Human Medicine, Medical
        Sciences)
IT   Diseases
        rheumatoid arthritis: connective tissue disease, immune system disease,
        joint disease
IT   Chemicals & Biochemicals
        autoantibodies; autoantigens; citrullinated proteins
IT   Alternate Indexing
        Arthritis, Rheumatoid (MeSH)
IT   Miscellaneous Descriptors
        apoptosis; autoantigenic posttranslational protein modifications;
        autoimmunity; citrullination; disease chronicity;
        immunopathogenesis
ORGN Super Taxa
        Animalia; Hominidae: Primates, Mammalia, Vertebrata, Chordata,
        Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
        animal (Animalia): experimental models; human (Hominidae): patient;
        mouse (Muridae): animal models
ORGN Organism Superterms
```

Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Primates; Rodents; Vertebrates

L3 ANSWER 2 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 2001:403532 BIOSIS
DN PREV200100403532
TI IgG reactivity against citrullinated myelin basic protein in multiple sclerosis.
AU de Seze, J. (1); Dubucquoi, S.; Lefranc, D.; Virecoulon, F.; Nuez, I.; Dutoit, V.; Vermersch, P.; Prin, L.
CS (1) Clinique Neurologique, Hopital R. Salengro, CHRU de Lille, 59037, Lille Cedex: j-deseze@chru-lille.fr France
SO Journal of Neuroimmunology, (July 2, 2001) Vol. 117, No. 1-2, pp. 149-155. print.
ISSN: 0165-5728.
DT Article
LA English
SL English
AB An increased level of citrullinated myelin basic protein (MBP-C8) has been reported in the brains of multiple sclerosis (MS) patients. However, the involvement of the immune response to post-translational modified MBP in the pathophysiology of MS remains speculative. The aim of this study was to compare the levels of immunoglobulin G antibodies to several MBP epitopes, before and after **citrullination**, in the cerebrospinal fluid (CSF) and sera of MS patients using enzyme-linked immunosorbent assay (ELISA). We analyzed antibody reactivity against various MBP-peptides in the CSF and sera of 60 MS patients, and 30 patients with other neurological diseases (OND) as controls. The peptides tested were: MBP75-98 (peptide 1), native (peptide 2) and citrullinated (peptide 3) MBP108-126 (ARG122fwdarwCit122), and native (peptide 4) and citrullinated (peptide 5) MBP151-170 (ARG159, 170fwdarwCit159,170). All selected peptides could support an immune reactivity in CSF and sera of MS and OND patients. A higher reactivity against peptide 4 was found in the CSF of MS patients compared with OND patients ($P<0.0001$), but not against citrullinated peptides (peptides 3 and 5). However, we observed that the **citrullination** state of peptide 2 modified the patterns of immune reactivity more markedly in MS patients ($P<0.0001$) than in OND patients ($P<0.02$). Although some MBP epitopes could be a potential target in MS, our data did not demonstrate any difference of antibody response to MBP peptides in their citrullinated forms.
CC Biochemical Studies - General *10060
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Nervous System - Physiology and Biochemistry *20504
Nervous System - Pathology *20506
Immunology and Immunochemistry - General; Methods *34502
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
BC Hominidae 86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Immune System (Chemical Coordination and Homeostasis); Nervous System (Neural Coordination)
IT Parts, Structures, & Systems of Organisms
brain: nervous system
IT Diseases
multiple sclerosis: immune system disease, nervous system disease, pathophysiology
IT Chemicals & Biochemicals
citrullinated myelin basic protein; immunoglobulin G: cerebrospinal fluid level, reactivity, serum level; myelin basic protein: **citrullination**
IT Alternate Indexing
Multiple Sclerosis (MeSH)
IT Methods & Equipment

ELISA: analytical method
IT Miscellaneous Descriptors
immune reactivity
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L3 ANSWER 3 OF 14 MEDLINE
AN 2001202210 MEDLINE
DN 21062442 PubMed ID: 11094435
TI **Citrullination**: a small change for a protein with great consequences for rheumatoid arthritis.
CM Comment on: Arthritis Res. 2000;2(2):101-14
AU van Venrooij W J; Pruijn G J
CS Department of Biochemistry, University of Nijmegen, Nijmegen, The Netherlands.. W.vanVenrooij@bioch.kun.nl
SO ARTHRITIS RESEARCH, (2000) 2 (4) 249-51. Ref: 20
Journal code: 100913255. ISSN: 1465-9905.
CY England: United Kingdom
DT Commentary
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200104
ED Entered STN: 20010417
Last Updated on STN: 20020707
Entered Medline: 20010412
AB A new autoantibody activity, which is almost 100% specific for rheumatoid arthritis (RA), has been found. The essential part of the B-cell epitope is a modified form of arginine (ie citrulline). The conversion of protein-contained arginine to citrulline is an enzymatic process that is carried out by peptidylarginine deiminase (PAD), an enzyme that appears to be hormonally controlled. Because of its remarkable specificity, **citrullination** and related processes might open new possibilities for studying the aetiology of RA.
CT Check Tags: Animal; Human
Apoptosis: PH, physiology
Arginine: ME, metabolism
*Arthritis, Rheumatoid: IM, immunology
*Arthritis, Rheumatoid: ME, metabolism
Autoantibodies: IM, immunology
*Autoantibodies: ME, metabolism
Autoantigens: IM, immunology
Autoantigens: ME, metabolism
Citrulline: IM, immunology
*Citrulline: ME, metabolism
RN 372-75-8 (Citrulline); 74-79-3 (Arginine)
CN 0 (Autoantibodies); 0 (Autoantigens)

L3 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 3
AN 2000:873602 CAPLUS
DN 135:91056
TI Insights into rheumatoid arthritis derived from the Sa immune system
AU Menard, Henri A.; Lapointe, Elvy; Rochdi, Moulay D.; Zhou, Zhi J.
CS Universite de Sherbrooke, Sherbrooke, QC, Can.
SO Arthritis Research [online computer file] (2000), 2(6), 429-432
CODEN: ARESFU; ISSN: 1465-9913
URL: http://www.arthritis-research.com/PDF/ar-2-6-429.pdf
PB Current Science Ltd.

DT Journal; General Review; (online computer file)
LA English
CC 15-0 (Immunochemistry)
AB A review with 31 refs. The Sa system is a recently described immune system that has a specificity and pos. predictive value of nearly 100% for rheumatoid arthritis (RA) in Asia, Europe, and the Americas. Its sensitivity of 30-40% suggests that it identifies a subset of RA patients. Anti-Sa antibodies are present from disease onset and are predictive of disease severity. The immune reactants are plentiful in the target tissue: antigen is present in the synovium, IgG antibody in the fluid. Immunol., Sa is a hapten-carrier antigen in which vimentin is the carrier and citrulline is the hapten. The **citrullination** of vimentin is closely related to apoptosis, and citrullinated vimentin is extremely sensitive to digestion by the ubiquitous calpains. Nevertheless, Sa is found in only a few cell lines. Calpastatin, the natural specific inhibitor of calpains, is also a RA-assocd., albeit non-specific, autoimmune system.
ST rheumatoid arthritis Sa autoantigen review
IT Antibodies
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(autoantibodies, anti-Sa; rheumatoid arthritis and Sa immune system)
IT Antigens
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(autoantigens, Sa; rheumatoid arthritis and Sa immune system)
IT Proteins, specific or class
Vimentins
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(citrullinated; rheumatoid arthritis and Sa immune system)
IT Diagnosis
Prognosis
Rheumatoid arthritis
(rheumatoid arthritis and Sa immune system)
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L3 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 2000:606022 CAPLUS
DN 134:206193
TI **Citrullination**: a small change for a protein with great consequences for rheumatoid arthritis
AU van Venrooij, Walther J.; Pruijn, Ger J. M.
CS University of Nijmegen, Nijmegen, Neth.
SO Arthritis Research [online computer file] (2000), 2(4), 249-251
CODEN: ARESFU; ISSN: 1465-9913
URL: http://arthritis-research.com/PDF/ar-2-4-249.pdf
PB Current Science Ltd.
DT Journal; General Review; (online computer file)
LA English
CC 15-0 (Immunochemistry)
AB A review with 20 refs. A new autoantibody activity, which is almost 100% specific for rheumatoid arthritis (RA), has been found. The essential part of the B-cell epitope is a modified form of arginine (i.e., citrulline). The conversion of protein-contained arginine to citrulline is an enzymic process that is carried out by peptidyl arginine deiminase (PAD), an enzyme that appears to be hormonally controlled. Because of its remarkable specificity, **citrullination** and related processes might open new possibilities for studying the etiol. of RA.
ST review citrulline rheumatoid arthritis **citrullination**
IT Rheumatoid arthritis
(**citrullination** in pathogenesis of rheumatoid arthritis)
IT 372-75-8, Citrulline
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(**citrullination** in pathogenesis of rheumatoid arthritis)
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; Manual of Biological Markers of Disease 1996
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L3 ANSWER 6 OF 14 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2001107026 EMBASE
TI **Citrullination**: A small change for a protein with great consequences for rheumatoid arthritis.
AU van Venrooij W.J.; Pruijn G.J.M.
CS W.J. van Venrooij, Department of Biochemistry, University of Nijmegen, PO Box 9101, Nijmegen HB-6500, Netherlands. W.vanVenrooij@bioch.kun.nl

SO Arthritis Research, (2000) 2/4 (249-251).
Refs: 20
ISSN: 1465-9905 CODEN: ARRECG
CY United Kingdom
DT Journal; Note
FS 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
031 Arthritis and Rheumatism
LA English
SL English
AB A new autoantibody activity, which is almost 100% specific for rheumatoid arthritis (RA), has been found. The essential part of the B-cell epitope is a modified form of arginine (ie citrulline). The conversion of protein-contained arginine to citrulline is an enzymatic process that is carried out by peptidylarginine deiminase (PAD), an enzyme that appears to be hormonally controlled. Because of its remarkable specificity, **citrullination** and related processes might open new possibilities for studying the aetiology of RA.
CT Medical Descriptors:
*rheumatoid arthritis: ET, etiology
B lymphocyte
protein processing
enzyme activity
hormonal regulation
apoptosis
mammal cell
human
nonhuman
human cell
animal cell
note
Drug Descriptors:
*citrulline: EC, endogenous compound
autoantibody: EC, endogenous compound
epitope: EC, endogenous compound
arginine: EC, endogenous compound
protein arginine deiminase: EC, endogenous compound
filaggrin
myelin basic protein: EC, endogenous compound
protein antibody: EC, endogenous compound
anticitrullinated protein antibody: EC, endogenous compound
autoantigen
vimentin
unclassified drug
RN (citrulline) 372-75-8; (arginine) 1119-34-2, 15595-35-4, 7004-12-8, 74-79-3; (protein arginine deiminase) 75536-80-0

L3 ANSWER 7 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 4
AN 2000:166258 BIOSIS
DN PREV200000166258
TI Cryoelectron microscopy of protein-lipid complexes of human myelin basic protein charge isomers differing in degree of **citrullination**.
AU Beniac, Daniel R.; Wood, D. Denise; Palaniyar, Nades; Ottensmeyer, F. Peter; Moscarello, Mario A.; Harauz, George (1)
CS (1) Department of Molecular Biology and Genetics and Biophysics Interdepartmental Group, University of Guelph, Guelph, ON, N1G 2W1 Canada
SO Journal of Structural Biology., (Feb., 2000) Vol. 129, No. 1, pp. 80-95.
ISSN: 1047-8477.
DT Article
LA English
SL English
AB Myelin basic protein (MBP) is considered to be essential for the maintenance of stability of the myelin sheath. Reduction in cationicity of

MBP, especially due to conversion of positively charged arginine residues to uncharged citrulline (Cit), has been found to be associated with multiple sclerosis (MS). Here, the interactions of an anionic phosphatidylserine/monosialoganglioside-GM1 (4:1, w:w) lipid monolayer with 18.5-kDa MBP preparations from age-matched adult humans without MS (no Cit residues), with chronic MS (6 Cit), and with acute Marburg-type MS (18 Cit) were studied by transmission and ultralow dose scanning transmission electron microscopy under cryogenic conditions. Immunogold labeling and single particle electron crystallography were used to define the nature of the complexes visualized. These electron microscopical analyses showed that the three different MBP charge isomers all formed uniformly sized and regularly shaped protein-lipid complexes with GM1, probably as hexamers, but exhibited differential association with and organization of the lipid. The least cationic Marburg MBP-Cit18 formed the most open protein-lipid complex. The data show a disturbance in lipid-MBP interactions at the ultrastructural level that is related to degree of **citrullination**, and which may be involved in myelin degeneration in multiple sclerosis.

CC Microscopy Techniques - Electron Microscopy *01058
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Lipids *10066
Nervous System - Physiology and Biochemistry *20504
Nervous System - Pathology *20506
Temperature: Its Measurement, Effects and Regulation - Cryobiology *23004
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508

IT Major Concepts
Biochemistry and Molecular Biophysics

IT Diseases
multiple sclerosis: immune system disease, nervous system disease

IT Chemicals & Biochemicals
human myelin basic protein: charge isomers, three-dimensional reconstruction; human myelin basic protein-lipid complex: **citrullination**; monosialoganglioside-Gm1; phosphatidylserine

IT Alternate Indexing
Multiple Sclerosis (MeSH)

IT Methods & Equipment
cryoelectron microscopy: microscopy method; single particle electron crystallography: analytical method; transmission electron microscopy: microscopy method

L3 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 2000:304097 CAPLUS
DN 133:190915
TI Fyn tyrosine kinase participates in the compact myelin sheath formation in the central nervous system
AU Seiwa, C.; Sugiyama, I.; Yagi, T.; Iguchi, T.; Asou, H.
CS Itabashi-ku, 35-2 Sakaecho, Department of Neurobiology, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan
SO Neuroscience Research (Shannon, Ireland) (2000), 37(1), 21-31
CODEN: NERADN; ISSN: 0168-0102
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
CC 13-3 (Mammalian Biochemistry)
Section cross-reference(s): 6

AB The cellular mechanisms for spiral wrapping and compaction of myelin sheaths by oligodendrocytes are not known yet. In this study, we examd. the role of fyn tyrosine kinase, which could be responsible for mol. events during the stage of myelination in the CNS. Western blot and immunohistochem. analyses revealed that fyn-deficient mice have significantly lower levels of myelin basic protein (MBP), which is required for intracellular membrane adhesion parts so-called major dense line (MDL) and thought to be essential for the stability of myelin sheath.

Electron microscopy verified that the myelin ultrastructure could be used to distinguish fyn-deficient mice from wild-type mice, showing a thin and redundant myelin sheath in the corpus callosum. Further, the electron-dense 'major' line in myelin from the purified myelin fractions remained condensed, and myelin compaction was split opened in fyn-deficient mice. To det. whether there was a change in the microheterogeneity of MBP due to a post-translational event we first investigated peptidylarginine deiminase (PAD), which is an enzyme that converts arginine residues in peptides to citrulline residues. PAD immunoreactivity was obsd. both in the myelin from fyn-deficient and wild-type mice. By Western blot anal. we found an increase of the citrullinated form of MBP. In addn., MBP from fyn-deficient mice did weakly induce vesicle aggregation properties of MBP-mediated adhesion. We concluded that although oligodendrocytes from fyn-deficient mice are able to wrap around the axon, they are unable to form compact myelin due to decreased MBP level and the presence of increased citrullinated MBP.

ST fyn kinase myelin compaction axon myelination oligodendrocyte brain development; myelin basic protein MBP **citrullination** peptidylarginine deiminase membrane phospholipid

IT Glycophosphoproteins
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(MAG (myelin-assocd. glycoprotein); fyn tyrosine kinase in compact myelin sheath formation in central nervous system)

IT Membrane, biological
(bilayer; fyn tyrosine kinase in compact myelin sheath formation in central nervous system)

IT Brain
(cerebral cortex; fyn tyrosine kinase in compact myelin sheath formation in central nervous system)

IT Brain
(cerebrum; fyn tyrosine kinase in compact myelin sheath formation in central nervous system)

IT Post-translational processing
(**citrullination** of MBP; fyn tyrosine kinase in compact myelin sheath formation in central nervous system)

IT Myelin
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process)
(compaction; fyn tyrosine kinase in compact myelin sheath formation in central nervous system)

IT Brain
(corpus callosum; fyn tyrosine kinase in compact myelin sheath formation in central nervous system)

IT Axon
Development, mammalian postnatal
Myelination
Oligodendrocyte
(fyn tyrosine kinase in compact myelin sheath formation in central nervous system)

IT Phosphatidylcholines, biological studies
Phosphatidylserines
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(fyn tyrosine kinase in compact myelin sheath formation in central nervous system in relation to)

IT Myelin basic protein
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(isoforms; fyn tyrosine kinase in compact myelin sheath formation in

central nervous system)
IT Brain
(putamen; fyn tyrosine kinase in compact myelin sheath formation in central nervous system)
IT 141349-87-3, Fyn kinase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(fyn tyrosine kinase in compact myelin sheath formation in central nervous system)
IT 60098-35-3, 2',3'-Cyclic nucleotide-3'-phosphohydrolase 75536-80-0, Peptidylarginine deiminase
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(fyn tyrosine kinase in compact myelin sheath formation in central nervous system in relation to)
IT 372-75-8, Citrulline
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(fyn tyrosine kinase in compact myelin sheath formation in central nervous system in relation to)
RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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L3 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2002 ACS
AN 2001:125902 CAPLUS
DN 134:337158
TI Biological significance of **citrullination** of arginine residues in proteins catalyzed by peptidylarginine deiminases
AU Asaga, Hiroaki
CS Department of Bioactivity Regulation, Tokyo Metropolitan Institute of Gerontology, Tokyo, 173-0015, Japan
SO Communications in Applied Cell Biology (2000), 17(1-4), 1-10
CODEN: CCBIE3; ISSN: 0913-8188
PB Oyo Saibo Seibutsugaku Kenkyukai
DT Journal; General Review
LA Japanese

CC 6-0 (General Biochemistry)
Section cross-reference(s): 13

AB A review with 44 refs., on protein deimination effects on various biol. reactions and processes. Although citrulline is not incorporated into proteins through the ordinary pathway of protein biosynthesis, its occurrence was unequivocally demonstrated about four decades ago. Citrulline residues were later shown to be formed by enzymic deimination of arginine residues by posttranslational modification enzymes, peptidylarginine deiminases (EC 3.5.3.15). Mammals have at least four types of the enzymes, designated type I, II, III, and IV. All the enzymes known to date show abs. requirements for calcium ion. To study biol. significance of this posttranslational modification, we developed sensitive method to detect citrulline residues on histol. sections and cell specimens as well as Western blot. By the use of this technique, we have obtained several lines of evidence, those of which suggest biol. significance of the protein deimination (**citrullination**). Protein deimination in the brain occurred in regions undergoing neurodegeneration and functions to deiminate various proteins including glial fibrillary acidic protein. Selective deimination of vimentin and prolactin release were concurrently occurring in calcium ionophore-treated anterior pituitary cells, suggesting the involvement of vimentin deimination to the event of prolactin release in lactotrophs. Such selective deimination of vimentin was also obsd. in calcium ionophore-induced apoptosis of mouse peritoneal macrophages. Immunocytochem. staining showed that localization of deiminated vimentin around the periphery of round-shaped nucleus, which was thought to be an early morphol. sign of apoptosis. Whereas, 70-kDa nuclear protein was selectively deiminated in calcium ionophore-induced apoptotic cell death of cultured rat epidermal keratinocytes. The **citrullination** might induce nuclear disassembly and promote apoptosis of these cells. In human epidermal tissue, major deiminated proteins were partially degraded keratin K1, while those from keratin K10 and keratin-assocd. protein filaggrin are minor components. Two citrulline residues were identified in V1 and V2 subdomains of mouse keratin K1. Based on these results, we speculate that the deimination might dissoc. of K1/K10, preexist K5/K14 networks or filaggrin in terminal differentiation of epidermis. Thus, biol. significance of **citrullination** seemed to be in neurodegeneration, nuclear disassembly in apoptosis, prolactin release, and terminal differentiation of epidermis. Some of the recent studies on the protein deimination reported from other groups were also discussed in this review.

ST review **citrullination** arginine protein peptidylarginine deiminases; deimination protein biol significance review

IT Proteins, general, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(biol. significance of **citrullination** of arginine residues in proteins catalyzed by peptidylarginine deiminases)

IT Imination
(protein deimination; biol. significance of **citrullination** of arginine residues in proteins catalyzed by peptidylarginine deiminases)

IT 75536-80-0, Peptidylarginine deiminase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(biol. significance of **citrullination** of arginine residues in proteins catalyzed by peptidylarginine deiminases)

IT 74-79-3, Arginine, biological studies 372-75-8, Citrulline
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(biol. significance of **citrullination** of arginine residues in proteins catalyzed by peptidylarginine deiminases)

L3 ANSWER 10 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 5

AN 1999:507627 BIOSIS
DN PREV199900507627
TI Rapid release and unusual stability of immunodominant peptide 45-89 from citrullinated myelin basic protein.
AU Cao, Ligong; Goodin, Richard; Wood, Denise; Moscarello, Mario A.; Whitaker, John N. (1)
CS (1) Department of Neurology, University of Alabama at Birmingham, Birmingham, AL, 35233-7340 USA
SO Biochemistry, (May 11, 1999) Vol. 38, No. 19, pp. 6157-6163. ISSN: 0006-2960.
DT Article
LA English
SL English
AB Myelin basic protein (MBP) exists in a population of isoforms and isomers. The 18.5 kDa MBP-C1, the main human adult isoform, has 170 residues and is relatively unmodified, whereas the same isoform can be citrullinated on six arginine residues to create the MBP-C8 (MBP Cit6) isomer. MBP Cit6 dominates in MS brain, accounting for 45% rather than 25% of the population of MBP isomers. In the fulminant form of MS, known as Marburg's Disease, 18 of the 19 arginines in MBP are citrullinated (MBP Cit18). **Citrullination** of MBP could lead to instability of myelin or limited remyelination. In this investigation, the susceptibilities to degradation by cathepsin D of MBP Cit6 and MBP-C1, both from normal and MS brain tissue, and Marburg MBP Cit18 were compared. The pattern of digestion was similar, and no differences of corresponding isomers in normal and MS brain were noted. However, normal MBP Cit6 was degraded 10-fold more rapidly than MBP-C1, and MBP Cit18 was degraded even more rapidly. MBP peptide 45-89 was preserved regardless of isomer type or source. Its generation was directly related to the citrulline content of the MBP substrate being 4 times faster in normal MBP Cit6 and 35 times faster in Marburg MBP Cit18 than in normal MBP-C1. Peptide 45-89 from a citrullinated MBP exhibited more deamidation, and, regardless of source, showed an alpha-helix structure in a lipid mimetic environment. We postulate that the generation of MBP peptides, including those that are dominant and encephalitogenic, is directly related to deimination of arginine to citrulline in MBP.
CC Biochemical Studies - General *10060
Nervous System - General; Methods *20501
BC Hominidae 86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Nervous System (Neural Coordination)
IT Chemicals & Biochemicals
citrullinated myelin basic protein: immunodominant peptide 45-89, structure
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L3 ANSWER 11 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:262832 BIOSIS
DN PREV199900262832
TI Rapid release and unusual stability of immunodominant peptide 45-89 from citrullinated MBP.
AU Cao, Ligong (1); Goodin, Richard (1); Wood, Denise; Moscarello, Mario A.; Whitaker, John N.
CS (1) Birmingham, AL USA
SO Neurology, (April 12, 1999) Vol. 52, No. 6 SUPPL. 2, pp. A400. Meeting Info.: 51st Annual Meeting of the American Academy of Neurology Toronto, Ontario, Canada April 17-24, 1999 American Academy of Neurology . ISSN: 0028-3878.

DT Conference
LA English
CC Biochemical Studies - General *10060
Nervous System - General; Methods *20501
Immunology and Immunochemistry - General; Methods *34502
General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
BC Hominidae 86215
IT Major Concepts
Biochemistry and Molecular Biophysics; Nervous System (Neural Coordination)
IT Parts, Structures, & Systems of Organisms
brain: nervous system
IT Diseases
multiple sclerosis: immune system disease, nervous system disease; Marburg's disease: nervous system disease
IT Chemicals & Biochemicals
peptide 45-89: immunodominant, release, stability; Marburg MBP-C8: **citrullination**, degradation; MBP [myelin basic protein]: **citrullination**; MBP-C1 [myelin basic protein-C1]
IT Alternate Indexing
Multiple Sclerosis (MeSH)
IT Miscellaneous Descriptors
Meeting Abstract; Meeting Poster
ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGN Organism Name
human (Hominidae)
ORGN Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L3 ANSWER 12 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 6
AN 1996:64773 BIOSIS
DN PREV199698636908
TI The effects of **citrullination** or variable amino-terminus acylation on the encephalitogenicity of human myelin basic protein in the PL/J mouse.
AU Zhou, Shan-Ren; Moscarello, Mario A.; Whitaker, John N. (1)
CS (1) Dep. Neurol. Center Neuroimmunol., University Alabama, Birmingham, AL 35294 USA
SO Journal of Neuroimmunology, (1995) Vol. 62, No. 2, pp. 147-152. ISSN: 0165-5728.
DT Article
LA English
AB The post-translational modifications of myelin basic protein (MBP) in the form of **citrullination** and varying length of amino-terminus acylation may modify the biological functions and immunological features of MBP. Both modifications influence the reaction of antibodies and specific T cells recognizing MBP. The present study was undertaken to compare the encephalitogenicity of the citrullinated isomer of MBP (MBP-C8) with the unmodified isomer of MBP (MBP-C1) and to determine if the length of amino-terminal acylation of MBP peptide 1-21 altered an encephalitogenic epitope. MBP-C8, whether from patients with or without multiple sclerosis (MS), and MBP-C1 could induce active experimental allergic encephalomyelitis (EAE) in PL/J mice. A trend of reduced severity of EAE was observed in MBP-C8-injected animals. An increase in the length of amino-terminus fatty acid decreased the encephalitogenicity of MBP peptide 1-21 for both active and adoptive EAE in PL/J mice. Only lymph node cells sensitive to MBP peptide acetyl 1-21 and butyl 1-21 could transfer clinical EAE. In adoptive EAE, MBP peptides hexyl and octyl 1-21 induced moderate histopathological but no clinical change, whereas MBP peptide decyl 1-21 caused neither. A broadening in the antibody response could be detected in the sera of mice with active EAE induced by

MBP-acylated peptides 1-21. Our findings demonstrate that encephalitogenicity is retained in the presence of **citrullination** but that the length of amino-terminus acylation diminishes the encephalitogenicity of MBP in the PL/J mouse. These findings may be relevant to MS where central nervous system myelin shows differences from normal in both MBP-C8 content and MBP amino-terminus acylation.

CC Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease *12508
Muscle - Pathology *17506
Nervous System - Pathology *20506
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
Allergy *35500

BC Hominidae 86215
Muridae *86375

IT Major Concepts
Allergy (Clinical Immunology, Human Medicine, Medical Sciences); Clinical Immunology (Human Medicine, Medical Sciences); Muscular System (Movement and Support); Neurology (Human Medicine, Medical Sciences); Pathology

IT Miscellaneous Descriptors
ALLERGIC ENCEPHALOMYELITIS; MULTIPLE SCLEROSIS; MYELIN BASIC PROTEIN

ORGN Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
Hominidae (Hominidae); Muridae (Muridae)

ORGN Organism Superterms
animals; chordates; humans; mammals; nonhuman mammals; nonhuman vertebrates; primates; rodents; vertebrates

L3 ANSWER 13 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 7

AN 1993:500476 BIOSIS

DN PREV199396124483

TI Immunological analysis of the amino terminal and the C8 isomer of human myelin basic protein.

AU Zhou, Shan-Ren (1); Whitaker, John N.; Wood, D. Denise; Moscarello, Mario A.

CS (1) Dep. Neurology, Univ. Ala. at Birmingham, Birmingham, AL 35294-0007 USA

SO Journal of Neuroimmunology, (1993) Vol. 46, No. 1-2, pp. 91-96. ISSN: 0165-5728.

DT Article

LA English

AB The **citrullination** and N-terminus acylation of myelin basic protein (MBP) increases the heterogeneity among the MBP isoforms. The present study was undertaken to further characterize the immune response to the citrullinated form (C8) of MBP as well as to the variably acylated N-terminus of BMP. Six well-characterized murine monoclonal antibodies (mAbs) to human MBP-C8 or MBP peptides (four mAbs to MBP acetyl 1-9, one mAb to MBP 10-19 and one mAb to MBP 80-89), one murine T cell line (PL11) to human MBP peptide acetyl 1-9 and one Lewis rat T cell line (RT-1) to guinea pig (GP) MBP peptide 68-88 were used to assess reactivity with MBP-C1, MBP-C8, and MBP peptides including a series of MBP peptide 1-21 containing 0, 2, 4, 6 8 or 10 carbon fatty acids. Enzyme-linked immunosorbent assay (ELISA) results revealed that all of the mAbs reacted with human MBP-C1 and MBP-C8 except anti-MBP 10-19 and anti-MBP-C8. The former reacted only with MBP-C1 and the latter only with MBP-C8. The presence and length of acylation of MBP peptide 1-21 modified reactivity. Three mAbs to MBP acetyl 1-9 reacted only with acetyl 1-21, and one mAb anti-MBP acetyl 1-9 reacted with all of MBP 1-21 preparations whether acylated or not. mAb anti-MBP-C8 generally reacted better with acylated

MBP 1-21 having longer fatty acid.s The PL11 T cell line strongly proliferated to human MBP-C1, MBP-C8 and MBP acetyl 1-9, responded but less well, to MBP 1-21 with longer fatty acids and failed to respond to nonacylated MBP peptide 1-21. The RT-1 cell line responded strongly to GP MBP peptide 68-88, marginally to MBP-C8 and failed to respond to MBP-C1 or any of the other MBP peptides. Specific immune responses to different MBP charge isomers and different N-terminal acylating groups of MBP may play a role in immune-mediated demyelination.

CC Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Lipids 10066
Biochemical Studies - Carbohydrates 10068
Biophysics - Molecular Properties and Macromolecules *10506
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Nervous System - Physiology and Biochemistry *20504
Nervous System - Pathology *20506
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508

BC Hominidae 86215
Caviidae 86300
Muridae *86375

IT Major Concepts
Biochemistry and Molecular Biophysics; Blood and Lymphatics (Transport and Circulation); Cell Biology; Clinical Immunology (Human Medicine, Medical Sciences); Nervous System (Neural Coordination); Neurology (Human Medicine, Medical Sciences)

IT Miscellaneous Descriptors
LYMPH NODE CELL; MENINGES; MYELIN BASIC PROTEIN; TRAFFICKING; WHITE MATTER

ORGN Super Taxa
Caviidae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
Caviidae (Caviidae); Hominidae (Hominidae); Muridae (Muridae)

ORGN Organism Superterms
animals; chordates; humans; mammals; nonhuman mammals; nonhuman vertebrates; primates; rodents; vertebrates

L3 ANSWER 14 OF 14 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1993:500477 BIOSIS
DN PREV199396124484
TI T lymphocyte lines and clones selected against synthetic myelin basic protein 82-102 peptide from Japanese multiple sclerosis patients.
AU Inobe, Jun-Ichi; Yamamura, Takashi; Kunishita, Tatsuhide; Tabira, Takeshi (1)
CS (1) Div. Demyelinating Div. Aging, Natl. Inst. Neurosci., NCNP, 4-1-1 Ogawahi-gashi, Kodaira, Tokyo 187 Japan
SO Journal of Neuroimmunology, (1993) Vol. 46, No. 1-2, pp. 83-90. ISSN: 0165-5728.
DT Article
LA English
AB As has been indicated in experimental autoimmune encephalomyelitis (EAE), the application of synthetic peptides or the selection of T cell lines may provide new insights into the pathogenesis of multiple sclerosis (MS). We report here on T cell lines/clones generated from peripheral blood of MS patients against an immunodominant myelin basic protein (MBP) peptide 82-102. This study demonstrates that the selection of T cell lines against the MBP peptide is much more efficient than against whole MBP in generating a large panel of T cell lines/clones, and therefore provides a powerful strategy for studying autoimmune T cell repertoire in individual subjects. The peptide-selected lines and clones recognized MBP 82-102,

shorter peptides MBP 89-101, 89-100 and guinea pig whole MBP mainly in the context of HLA-DR, but did not cross-recognize virus-derived peptides homologous to MBP 82-102. Seven out of ten clones were found to recognize MBP 82-102 in the absence of autologous antigen presenting cells (APC), and in three of the seven clones, specificity for MBP 82-102 could be demonstrated only in the absence of APC because of their strong reactivity against autologous APC. Two-color flow cytometry revealed that the clones were heterogeneous with regard to expression of CD4 and CD8 molecules. Overall, the clones selected by the peptide were rather heterogeneous in phenotype and function compared with those selected by whole MBP.

CC Cytology and Cytochemistry - Human *02508
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease *12508
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Nervous System - Pathology *20506
Virology - Animal Host Viruses 33506
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
Allergy *35500

BC Animal Viruses - General 02600
Hominidae 86215
Caviidae *86300

IT Major Concepts
Allergy (Clinical Immunology, Human Medicine, Medical Sciences); Blood and Lymphatics (Transport and Circulation); Cell Biology; Clinical Immunology (Human Medicine, Medical Sciences); Neurology (Human Medicine, Medical Sciences); Pathology

IT Miscellaneous Descriptors
ACYLATION; **CITRULLINATION**; DEMYELINATION; FATTY ACID; GUINEA-PIG; MONOCLONAL ANTIBODY; MULTIPLE SCLEROSIS; T CELL

ORGN Super Taxa
Animal Viruses - General: Viruses; Caviidae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
animal viruses (Animal Viruses - General); mouse (Muridae); rat (Muridae); Caviidae (Caviidae); Hominidae (Hominidae)

ORGN Organism Superterms
animals; chordates; humans; mammals; microorganisms; nonhuman mammals; nonhuman vertebrates; primates; rodents; vertebrates; viruses

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